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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,492	01/27/2006	Kenneth Kinzler	001107.00514	4914
22907 7590 06/14/2007 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051			EXAMINER CHUNDURU, SURYAPRABHA	
			ART UNIT 1637	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/516,492	Applicant(s) KINZLER ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/1/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status

1. Claims 1-35 are pending and considered for examination in this office action.

Priority

2. This application filed on January 27, 2006 is a 371 of PCT/US03/17262 filed on 6/04/2003, which claims benefit of US provisional application 60/385,901 filed on 6/6/2002.

Information Disclosure Statement

3. The Information Disclosure Statement filed on December 1, 2004 has been considered.

Informalities

4. The following informalities are noted:
 - (i) Claim 32 is incomplete and does not end with a period.
 - (ii) Claim 33 is incomplete and improper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 34 and 33 are incomplete and unclear because the meets and bounds are unclear. It is unclear because claim 33 does not recite a last step how the allelic expression is measured and claim 33 is incomplete because it is not clear to what first individual the comparison is performed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1-6, 9-16, and 34-35 are rejected under 35 U.S.C.102 (b) as being anticipated by Lapidus et al. (US 5,928,870).

Lapidus et al. teach a method of claim 1, 34-35 associating genotype with a phenotype (cancer) comprising (i) determining levels of expression of alleles (enumerate amount of gene or genes or mutation in a genetic region) in a first population (sample) (see col. 2, line 58-60, col. 3, line 11-15); (ii) comparing the levels of expression of alleles with a second population (known control sample); identifying the levels of expression of alleles whose expression differs statistically significant manner between the first and second population as having an association with the phenotype (see col. 2, line 60-67, col. 3, line 15-27, col. 5, line 30-50, col. 7, line 42-53, col. 8, line 25-67, col. 9, line 1-11).

With regard to claims 2-6, and 13-15, Lapidus et al. also teach (a) that the phenotype comprises, disease susceptibility or a disease (cancer or precancer), birth defects (metabolic error), status of heterozygosity of an allele, sequence variation including insertion, deletion, SNP (see col. 2, line 39-57, col. 9, line 45-62).

With regard to claim 9-12, Lapidus et al. teach that the phenotype is not related to a known

disease (precancerous), heritable allele (mutation is heritable), determining haplotype (see col. 7, line 42-53, col. 8, line 25-67, col. 9, line 1-11).

With regard to claim 16, Lapidus et al. teach that the method further comprises determining the level of expression of at least one other allele of the gene (see col. 9, line 66-67, col. 10, line 1-9). Accordingly Lapidus et al. anticipates the instant claims.

B. Claims 1-15, 17, 19-20, 22-33 are rejected under 35 U.S.C.102 (b) as being anticipated by Lapidus et al. (US 6,146,828).

Lapidus et al. teach a method of claim 1, 19, 32-33, for measuring allelic expression variation in a non-imprinted individual or first sample population, and a reference sample comprising (i) reverse transcribing and amplifying mRNA from individuals to form a first cDNA and a second cDNA (see col. 2, line 42-67, col. 3, line 7-28, col. 4, line 20-67, col. 5, line 1-19, col. 6, line 15-45, col. 7, line 1-38); (ii) hybridizing primers to cDNA and labeling the primers using single base extension (see col. 3, line 7-28, col. 7, line 7-67); (iii) comparing the amounts of differentially labeled primers, wherein the statistically significant difference between the first and second primers are indicative of first and second alleles and indicative of the correlation between two samples (see col. 4, line 20-67, col. 5, line 1-19, col. 6, line 64-67, see col. 12, line 15-60).

With regard to claims 2-6, and 13-15, 28-31, Lapidus et al. also teach (a) that the phenotype comprises, disease susceptibility or a disease (cancer or precancer), status of heterozygosity of an allele, sequence variation including deletion, single base polymorphisms (see col. 3, line 51-62).

With regard to claim 7-12, 27, Lapidus et al. teach that the phenotype is not related to a

known disease (precancerous), heritable allele (mutation is heritable), polymorphic phenotype (microsatellite rearrangement) determining allele expression and determining haplotype (see col. 6, line 15-45).

With regard to claims 17, 20, 22, Lapidus et al. also teach differential labeling using fluorescent dye terminators (see col. 10, line 22-38) and single base extension (see col. 7, line 7-21).

With regard to claims 23-26, Lapidus teach detecting allele expression alteration in expression variation in parent offspring and correlating variation as heritable, statistically significant difference at least 20% (see col. 3, line 46-49, col. 5, line 20-62, col. 6, line 16-32). Accordingly Lapidus et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapidus et al. (USPN. 6,146,828) ('828) in view of Lapidus et al. (USPN. 5,928,870).

Lapidus et al. ('828) teach a method of associating a genotype with a phenotype as discussed above in section 6B.

However, Lapidus et al ('828) did not specifically teach capillary electrophoresis to compare the allelic variation.

Lapidus et al. ('870) teach a method of associating a genotype with a phenotype, wherein the method comprises comparing the allelic sequence variation using a capillary gel electrophoresis (see col. 5, line 9-21).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method associating a genotype with a phenotype as taught by Lapidus et al. ('870) with incorporation of comparing the variation by capillary electrophoresis as taught by Lapidus et al. ('870) to achieve expected advantage of developing a cost-effective qualitative and quantitative method for detecting variation between two samples. An ordinary practitioner would have been motivated to modify the method as taught by ('828) with the incorporation size separation electrophoresis as taught by ('870) because an ordinary practioner skilled in the art would have a reasonable expectation of success that the combination would result in a sensitive cost-effective method for qualitative and quantitative

analysis of allelic variation because Lapidus et al. ('870) explicitly taught size separation of allelic variation using capillary gel electrophoresis in determining allelic size variation between two samples (see col. 5, line 9-21) and such a modification of the method is considered obvious over cited prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Suryaprabha Chunduru
SURYAPRABHA CHUNDURU 6/11/07
PRIMARY EXAMINER